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L6 and l4	604

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<u>L7</u>	L6 and l4	604	<u>L7</u>
<u>L6</u>	mmtv near4 (promoter or promotor or regulatory adj element)	837	<u>L6</u>
<u>L5</u>	l3 and l4	72	<u>L5</u>
<u>L4</u>	retrovir\$ or adenovir\$	23073	<u>L4</u>
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<u>L2</u>	vector or virus or particle	595797	<u>L2</u>
<u>L1</u>	(whey adj acidic adj protein or wap) near3 (promoter or promotor or regulatory adj element)	94	<u>L1</u>

END OF SEARCH HISTORY

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- ☐ 21. [6395958](#). 15 Jul 99; 28 May 02. Method of producing a polypeptide in an ungulate. Strelchenko; Nikolai S., et al. 800/7; 800/15 800/16 800/17 800/24. C12P021/00 A01K067/027 C12N015/00.
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- ☐ 22. [6361991](#). 02 Nov 99; 26 Mar 02. Targeting gene expression to living tissue using jet injection. Furth; Priscilla Anne, et al. 435/285.3; 128/200.14 600/104 604/70 606/119. C12M003/00.
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- ☐ 23. [6361968](#). 26 Jun 99; 26 Mar 02. Extension of a protein-protein interaction surface to inactive the function of a cellular protein. Vinson; Charles R., et al. 435/69.1; 530/300 530/350. C12P021/02 C07K019/00.
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- ☐ 24. [6350615](#). 31 Mar 00; 26 Feb 02. Gene product over expressed in cancer cells. Kaufman; Russel E., et al. 436/86; 530/350. G01N033/00.
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- ☐ 27. [6330472](#). 29 Jan 99; 11 Dec 01. Prophylactic and therapeutic treatment of the ductal epithelium for a mammary gland for cancer. Sukumar; Saraswati Vaidyanathan. 604/21; 514/1 514/2. A61N001/30 A61K031/00.
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- ☐ 28. [6323008](#). 14 Aug 97; 27 Nov 01. Methods for producing sialyloligosaccharides in a dairy source. Pelletier; Marc, et al. 435/84; 435/101 435/274 435/99 536/124 536/127. C12P019/26.
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- ☐ 29. [6287863](#). 09 Nov 95; 11 Sep 01. Method of transferring a DNA sequence to a cell in vitro. Hodgson; Clague P.. 435/455; 435/400 435/456 514/44 800/19 800/23. C12N015/85 C12N015/00.
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- ☐ 31. [6268211](#). 20 Aug 91; 31 Jul 01. Non-infectious HIV transgene. Jolicoeur; Paul. 435/320.1; 435/325 435/455 435/69.1 435/91.2 536/23.72. C12N015/63 C12N015/09 C12N015/00 C12N005/00.
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- ☐ 32. [6262336](#). 28 May 99; 17 Jul 01. Expression of a heterologous protein C in mammary tissue of transgenic animals using a long whey acidic protein promoter. Lubon; Henryk, et al. 800/14; 536/24.1 800/15 800/16 800/17 800/18 800/7. A01K067/027 C12P021/00 C07H021/04.
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- ☐ 33. [6255554](#). 04 Mar 99; 03 Jul 01. Transgenic non-human mammals expressing human coagulation factor VIII and von Willebrand factor. Lubon; Henryk, et al. 800/14; 435/69.6 800/15 800/16 800/17 800/18 800/25 800/7. A01K067/027 C12P021/00 C12P021/04 C12N015/00.

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- ☒ 34. 6241982. 06 Jun 95; 05 Jun 01. Method for treating brain cancer with a conditionally lethal gene. Barber; Jack R., et al. 424/93.2; A61K048/00.
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- ☐ 35. 6217860. 24 Sep 99; 17 Apr 01. Gene therapy for solid tumors, papillomas and warts. Woo; Savio L. C., et al. 424/93.2; 424/93.6 435/320.1 514/44. A01K063/00 A61K038/00 A61K048/00 C12N015/00.
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- ☐ 36. 6153184. 08 Jun 98; 28 Nov 00. Destruction of the epithelium of an exocrine gland in the prophylactic and therapeutic treatment of cancer. Sukumar; Saraswati Vaidyanathan. 424/93.6; 424/93.1 424/93.2 435/455 514/2 514/44. A01N063/00.
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- ☐ 37. 6072034. 14 Dec 98; 06 Jun 00. Gene product over expressed in cancer cells. Kaufman; Russel E., et al. 530/350; 435/252.33 435/320.1 435/69.1 530/300 536/23.5. C07K001/00 A61K038/00.
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- ☐ 38. 6066624. 15 Feb 96; 23 May 00. Gene therapy for solid tumors using adenoviral vectors comprising suicide genes and cytokine genes. Woo; Savio L. C., et al. 514/44; 424/93.2. A61K048/00.
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- ☐ 40. 6025540. 07 Dec 95; 15 Feb 00. Transgenic non-human mammals producing EC-SOD protein in their milk. Hansson; Lennart. 800/14; 800/23 800/25 800/4 800/7 800/8. C12N005/00 C12N015/00 A01K067/00 C12P021/00.
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Terms	Documents
13 and 14	72

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=> d his

(FILE 'HOME' ENTERED AT 16:30:27 ON 07 NOV 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 16:30:45 ON 07 NOV 2002

L1 476 S (WHEY(W)ACIDIC(W)PROTEIN OR WAP) (5A) (PROMOTER OR PROMOTOR OR  
L2 425 S (WHEY(W)ACIDIC(W)PROTEIN OR WAP) (3A) (PROMOTER OR PROMOTOR OR  
L3 115 S (VECTOR OR VIRUS OR PARTICLE) AND L2  
L4 66 DUP REM L3 (49 DUPLICATES REMOVED)

=> d au ti so 30-66 l4

L4 ANSWER 30 OF 66 CAPLUS COPYRIGHT 2002 ACS  
AU Lu, Yifan; Deng, Jixian; Xiao, Chengzu; Ma, Qingjun  
TI WAP gene identification and construction of **vectors** expressing  
human G-CSF in mammary gland  
SO Zhongguo Shouyi Xuebao (1998), 18(5), 441-444  
CODEN: ZSXUF5; ISSN: 1005-4545

L4 ANSWER 31 OF 66 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 10  
AU Husler, Margaret R.; Kotopoulis, Kristin A.; Sundberg, John P.; Tennent,  
Barbara J.; Kunig, Sabine V.; Knowles, Barbara B.  
TI Lactation-induced WAP-SV40 Tag transgene expression in C57BL/6J mice leads  
to mammary carcinoma  
SO Transgenic Research (1998), 7(4), 253-263  
CODEN: TRSEES; ISSN: 0962-8819

L4 ANSWER 32 OF 66 CAPLUS COPYRIGHT 2002 ACS  
IN Gunzburg, Walter H.; Karle, Peter; Saller, Robert Michael  
TI Cytochrome P450 encoding retroviral **vectors** and their use as  
antitumor agents  
SO PCT Int. Appl., 25 pp.  
CODEN: PIXXD2

L4 ANSWER 33 OF 66 CAPLUS COPYRIGHT 2002 ACS  
IN Guenzburg, Walter H.; Saller, Robert Michael; Salmons, Brian  
TI Rodent whey acid protein (WAP) or mouse mammary tumor **virus**  
(MMTV) regulatory sequences for targeted expression of heterologous genes  
in human mammary cells and applications in carcinoma gene therapy  
SO PCT Int. Appl., 46 pp.  
CODEN: PIXXD2

L4 ANSWER 34 OF 66 MEDLINE DUPLICATE 11  
AU Wagner K U; Wall R J; St-Onge L; Gruss P; Wynshaw-Boris A; Garrett L; Li  
M; Furth P A; Hennighausen L  
TI Cre-mediated gene deletion in the mammary gland.  
SO NUCLEIC ACIDS RESEARCH, (1997 Nov 1) 25 (21) 4323-30.  
Journal code: 0411011. ISSN: 0305-1048.

L4 ANSWER 35 OF 66 CAPLUS COPYRIGHT 2002 ACS  
AU Lu, Y. F.; Deng, J. X.; Xiao, C. Z.; Ma, Q. J.; Zhou, J.  
TI Expression of human G-CSF in mammary gland of mice by injecting plasmid  
DNA  
SO Proceedings of International Conference on Animal Biotechnology, Beijing,  
June 11-14, 1997 (1997), 400-402. Editor(s): Li, Ning; Chen, Yongfu.  
Publisher: International Academic Publishers, Beijing, Peop. Rep. China.  
CODEN: 68CNAB

L4 ANSWER 36 OF 66 CAPLUS COPYRIGHT 2002 ACS  
AU Jura, Jacek; Smorag, Zdzislaw; Katska, Lucyna; Skrzyszowska, Maria;  
Houdebine, Louis-Marie; Rynska, Bozena  
TI Influence of DNA concentration on the efficiency of bovine blastocyst

- production after WAP-bGH microinjection into germinal vesicle of immature oocytes, zygotes and embryos obtained in vivo or in vitro  
SO Biotechnologia (1997), (4), 71-81  
CODEN: BIECEV; ISSN: 0860-7796
- L4 ANSWER 37 OF 66 CAPLUS COPYRIGHT 2002 ACS  
IN Guenzburg, Walter H.; Salmons, Brian  
TI Viral and plasmid **vectors** encoding mouse mammary tumor  
**virus** Naf repressor or Sag antigen for control of viral infections  
or lymphocyte gene therapy  
SO PCT Int. Appl., 44 pp.  
CODEN: PIXXD2
- L4 ANSWER 38 OF 66 CAPLUS COPYRIGHT 2002 ACS  
IN Guenzburg, Walter H.; Winder, David; Saller, Robert Michael  
TI **Vectors** carrying therapeutic genes encoding antimicrobial  
peptides for gene therapy  
SO PCT Int. Appl., 54 pp.  
CODEN: PIXXD2
- L4 ANSWER 39 OF 66 CAPLUS COPYRIGHT 2002 ACS  
IN Lubron, Henryk; Drohan, William N.; Velander, William H.  
TI Transgenic animals expressing genes for human coagulation factor VIII and  
von willebrand factor with secretion of the protein into milk  
SO PCT Int. Appl., 28 pp.  
CODEN: PIXXD2
- L4 ANSWER 40 OF 66 CAPLUS COPYRIGHT 2002 ACS  
IN Guenzburg, Walter Henry; Saller, Robert Michael  
TI Safe, non-self-inactivating retroviral expression **vectors** using  
non-LTR promoters for gene therapy  
SO PCT Int. Appl., 40 pp.  
CODEN: PIXXD2
- L4 ANSWER 41 OF 66 CAPLUS COPYRIGHT 2002 ACS  
AU Yarus, S.; Rosen, J. M.; Cole, A. M.; Diamond, G.  
TI Production of active bovine tracheal antimicrobial peptide in milk of  
transgenic mice  
SO Proceedings of the National Academy of Sciences of the United States of  
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CODEN: PNASA6; ISSN: 0027-8424
- L4 ANSWER 42 OF 66 MEDLINE DUPLICATE 12  
AU Gallahan D; Jhappan C; Robinson G; Hennighausen L; Sharp R; Kordon E;  
Callahan R; Merlino G; Smith G H  
TI Expression of a truncated Int3 gene in developing secretory mammary  
epithelium specifically retards lobular differentiation resulting in  
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SO CANCER RESEARCH, (1996 Apr 15) 56 (8) 1775-85.  
Journal code: 2984705R. ISSN: 0008-5472.
- L4 ANSWER 43 OF 66 MEDLINE DUPLICATE 13  
AU Santarelli R; Tzeng Y J; Zimmermann C; Guhl E; Graessmann A  
TI SV40 T-antigen induces breast cancer formation with a high efficiency in  
lactating and virgin WAP-SV-T transgenic animals but with a low efficiency  
in ovariectomized animals.  
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- L4 ANSWER 44 OF 66 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 14  
AU Kilty, Iain C.; Rudland, Philip S.; Barraclough, Roger  
TI Hormonal control of transcription from two mammary specific promoters in a  
rat mammary epithelial cell line  
SO Biochemical Society Transactions (1996), 24(3), 351S

- L4 ANSWER 45 OF 66 MEDLINE DUPLICATE 15  
 AU Attal J; Cajero-Juarez M; Petitclerc D; Theron M C; Stinnakre M G;  
 Bearzotti M; Kann G; Houdebine L M  
 TI The effect of matrix attached regions (MAR) and specialized chromatin  
 structure (SCS) on the expression of gene constructs in cultured cells and  
 in transgenic mice.  
 SO MOLECULAR BIOLOGY REPORTS, (1995-96) 22 (1) 37-46.  
 Journal code: 0403234. ISSN: 0301-4851.
- L4 ANSWER 46 OF 66 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 16  
 AU Li, Minglin; Hu, Jiadi; Heermeier, Kathrin; Hennighausen, Lothar; Furth,  
 Priscilla A.  
 TI Expression of a viral oncoprotein during mammary gland development alters  
 cell fate and function: induction of p53-independent apoptosis is followed  
 by impaired milk protein production in surviving cells  
 SO Cell Growth & Differentiation (1996), 7(1), 3-11  
 CODEN: CGDIE7; ISSN: 1044-9523
- L4 ANSWER 47 OF 66 CAPLUS COPYRIGHT 2002 ACS  
 IN Woo, Savio L. C.; Chen, Shu-Hsia  
 TI Adenovirus-carried suicide gene and prodrug for gene therapy for solid  
 tumors, papillomas and warts  
 SO PCT Int. Appl., 77 pp.  
 CODEN: PIXXD2
- L4 ANSWER 48 OF 66 CAPLUS COPYRIGHT 2002 ACS  
 IN Hansson, Lennart  
 TI Production and secretion of human extracellular superoxide dismutase into  
 milk of transgenic mammals  
 SO PCT Int. Appl., 102 pp.  
 CODEN: PIXXD2
- L4 ANSWER 49 OF 66 MEDLINE DUPLICATE 17  
 AU Kolb A F; Albang R; Brem G; Erfle V; Gunzburg W H; Salmons B  
 TI Characterization of a protein that binds a negative regulatory element in  
 the mammary-specific **whey acidic protein**  
**promoter**.  
 SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1995 Dec 26) 217 (3)  
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- L4 ANSWER 50 OF 66 MEDLINE DUPLICATE 18  
 AU Petitclerc D; Attal J; Theron M C; Bearzotti M; Bolifraud P; Kann G;  
 Stinnakre M G; Pointu H; Puissant C; Houdebine L M  
 TI The effect of various introns and transcription terminators on the  
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 and in the mammary gland of transgenic mice.  
 SO JOURNAL OF BIOTECHNOLOGY, (1995 Jun 21) 40 (3) 169-78.  
 Journal code: 8411927. ISSN: 0168-1656.
- L4 ANSWER 51 OF 66 MEDLINE DUPLICATE 19  
 AU Welte T; Garimorth K; Philipp S; Jennewein P; Huck C; Cato A C; Doppler W  
 TI Involvement of Ets-related proteins in hormone-independent mammary  
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 SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1994 Aug 1) 223 (3) 997-1006.  
 Journal code: 0107600. ISSN: 0014-2956.
- L4 ANSWER 52 OF 66 MEDLINE DUPLICATE 20  
 AU Hennighausen L; McKnight R; Burdon T; Baik M; Wall R J; Smith G H  
 TI Whey acidic protein extrinsically expressed from the mouse mammary tumor  
**virus** long terminal repeat results in hyperplasia of the  
 coagulation gland epithelium and impaired mammary development.

SO CELL GROWTH AND DIFFERENTIATION, (1994 Jun) 5 (6) 607-13.  
Journal code: 9100024. ISSN: 1044-9523.

L4 ANSWER 53 OF 66 CAPLUS COPYRIGHT 2002 ACS  
AU Kim, J. H.; Utsumi, K.; Iritani, A.; Lee, H. T.; Chung, K. S.  
TI Characterization of morphological abnormalities in transgenic mice  
expressing the human erythropoietin gene  
SO Molecules and Cells (1994), 4(4), 381-6  
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L4 ANSWER 54 OF 66 SCISEARCH COPYRIGHT 2002 ISI (R)  
AU KOLB A F; GUNZBURG W H; ALBANG R; BREM G; ERFLE V; SALMONS B (Reprint)  
TI NEGATIVE REGULATORY ELEMENT IN THE MAMMARY SPECIFIC **WHEY**  
**ACIDIC PROTEIN PROMOTER**  
SO JOURNAL OF CELLULAR BIOCHEMISTRY, (OCT 1994) Vol. 56, No. 2, pp. 245-261.  
ISSN: 0730-2312.

L4 ANSWER 55 OF 66 CAPLUS COPYRIGHT 2002 ACS  
IN Furth, Priscilla Anne; Hennighausen, Lothar  
TI Targeting gene expression to living tissue using jet injection  
SO PCT Int. Appl., 37 pp.  
CODEN: PIXXD2

L4 ANSWER 56 OF 66 CAPLUS COPYRIGHT 2002 ACS  
IN Hansson, Lennart; Stroemqvist, Mats; Bergstroem, Sven; Hernell, Olle;  
Toernell, Jan  
TI DNA encoding .kappa.-casein, manufacture of the protein with recombinant  
cells or transgenic mammals, and milk or infant formula containing the  
protein  
SO PCT Int. Appl., 124 pp.  
CODEN: PIXXD2

L4 ANSWER 57 OF 66 MEDLINE DUPLICATE 21  
AU Mehig C S; Elias V D; Mehig R J; Helferich W G; Tucker H A  
TI Development of a recombinant bovine leukemia **virus**  
**vector** for delivery of a synthetic bovine growth hormone-releasing  
factor gene into bovine cells.  
SO JOURNAL OF ANIMAL SCIENCE, (1993 Mar) 71 (3) 687-93.  
Journal code: 8003002. ISSN: 0021-8812.

L4 ANSWER 58 OF 66 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
AU Cardiff, Robert D. (1); Muller, William J.  
TI Transgenic mouse models of mammary tumorigenesis.  
SO Lemoine, N. R. [Editor]; Wright, N. A. [Editor]. Cancer Surveys, (1993)  
Vol. 16, pp. 97-113. Cancer Surveys; The molecular pathology of cancer.  
Publisher: Cold Spring Harbor Laboratory Press 10 Skyline Drive,  
Plainview, New York 11803, USA.  
ISSN: 0261-2429. ISBN: 0-87969-389-4.

L4 ANSWER 59 OF 66 SCISEARCH COPYRIGHT 2002 ISI (R)  
AU WELTE T; PHILIPP S; CAIRNS C; GUSTAFSSON J A; DOPPLER W (Reprint)  
TI GLUCOCORTICOID RECEPTOR-BINDING SITES IN THE PROMOTER REGION OF MILK  
PROTEIN GENES  
SO JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, (DEC 1993) Vol. 47,  
No. 1-6, pp. 75-81.  
ISSN: 0960-0760.

L4 ANSWER 60 OF 66 CAPLUS COPYRIGHT 2002 ACS  
AU Dale, Trevor C.; Krnacik, Michael J.; Schmidhauser, Christian; Yang,  
Claudia L. Q.; Bissell, Mina J.; Rosen, Jeffrey M.  
TI High-level expression of the rat whey acidic protein gene is mediated by  
elements in the promoter and 3' untranslated region  
SO Molecular and Cellular Biology (1992), 12(3), 905-14  
CODEN: MCEBD4; ISSN: 0270-7306

L4 ANSWER 61 OF 66 MEDLINE DUPLICATE 22  
 AU Ebert K M; Selgrath J P; DiTullio P; Denman J; Smith T E; Memon M A;  
 Schindler J E; Monastersky G M; Vitale J A; Gordon K  
 TI Transgenic production of a variant of human tissue-type plasminogen  
 activator in goat milk: generation of transgenic goats and analysis of  
 expression.  
 SO BIO/TECHNOLOGY, (1991 Sep) 9 (9) 835-8.  
 Journal code: 8309273. ISSN: 0733-222X.

L4 ANSWER 62 OF 66 SCISEARCH COPYRIGHT 2002 ISI (R)  
 AU GUNZBURG W H; SALMONS B (Reprint); ZIMMERMANN B; MULLER M; ERFLE V; BREM G  
 TI A MAMMARY-SPECIFIC PROMOTER DIRECTS EXPRESSION OF GROWTH-HORMONE NOT ONLY  
 TO THE MAMMARY-GLAND, BUT ALSO TO BERGMAN GLIA CELLS IN TRANSGENIC MICE  
 SO MOLECULAR ENDOCRINOLOGY, (1991) Vol. 5, No. 1, pp. 123-133.

L4 ANSWER 63 OF 66 CAPLUS COPYRIGHT 2002 ACS  
 AU Henninghausen, Lothar; Furth, Priscilla A.; Pittius, Christoph W.  
 TI .kappa.B elements strongly activate gene expression in non-lymphoid cells  
 and function synergistically with NF1 elements  
 SO Nucleic Acids Research (1989), 17(20), 8197-206  
 CODEN: NARHAD; ISSN: 0305-1048

L4 ANSWER 64 OF 66 CAPLUS COPYRIGHT 2002 ACS  
 AU Gordon, Katherine; Vitale, James; Lee, Eric; Westphal, Heiner;  
 Hennighausen, Lothar  
 TI Expression of human TPA in the milk of transgenic animals  
 SO UCLA Symposia on Molecular and Cellular Biology, New Series (1989),  
 87(Gene Transfer Gene Ther.), 57-66  
 CODEN: USMBD6; ISSN: 0735-9543

L4 ANSWER 65 OF 66 MEDLINE  
 AU Pittius C W; Hennighausen L; Lee E; Westphal H; Nicols E; Vitale J; Gordon  
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 TI A milk protein gene promoter directs the expression of human tissue  
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 SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF  
 AMERICA, (1988 Aug) 85 (16) 5874-8.  
 Journal code: 7505876. ISSN: 0027-8424.

L4 ANSWER 66 OF 66 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
 AU Attal, Joe; Cajero-Juarez, Marco; Petitclerc, Denis; Theron, Marie-Claire;  
 Stinnakre, Marie-Georges; Bearzotti, Monique; Kann, Guy; Houdebine,  
 Louis-Marie (1)  
 TI The effect of matrix attached regions (MAR) and specialized chromatin  
 structure (SCS) on the expression of gene constructs in cultured cells and  
 in transgenic mice.  
 SO Molecular Biology Reports, Vol. 22, No. 1, pp. 37-46.  
 ISSN: 0301-4851.

=> d bib 47 48 l4

L4 ANSWER 47 OF 66 CAPLUS COPYRIGHT 2002 ACS  
 AN 1995:494727 CAPLUS  
 DN 122:230771  
 TI Adenovirus-carried suicide gene and prodrug for gene therapy for solid  
 tumors, papillomas and warts  
 IN Woo, Savio L. C.; Chen, Shu-Hsia  
 PA Baylor College of Medicine, USA  
 SO PCT Int. Appl., 77 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English



FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9505835	A1	19950302	WO 1994-US9784	19940825
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5631236	A	19970520	US 1993-112745	19930826
	CA 2169260	AA	19950302	CA 1994-2169260	19940825
	AU 9476776	A1	19950321	AU 1994-76776	19940825
	AU 677430	B2	19970424		
	EP 719147	A1	19960703	EP 1994-927282	19940825
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09504784	T2	19970513	JP 1994-507792	19940825
	US 6066624	A	20000523	US 1996-600942	19960215
	US 6217860	B1	20010417	US 1999-404614	19990924
PRAI	US 1993-112745	A	19930826		
	WO 1994-US9784	W	19940825		
	US 1996-600942	A3	19960215		

L4 ANSWER 48 OF 66 CAPLUS COPYRIGHT 2002 ACS

AN 1995:501316 CAPLUS

DN 122:237909

TI Production and secretion of human extracellular superoxide dismutase into milk of transgenic mammals

IN Hansson, Lennart

PA Symbicom AB, Swed.

SO PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9500637	A1	19950105	WO 1994-IB181	19940624
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, CZ, DE, DE, DK, DK, FI, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, SK, TJ, TT, UA, US, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2164089	AA	19950105	CA 1994-2164089	19940624
	AU 9469356	A1	19950117	AU 1994-69356	19940624
	AU 687068	B2	19980219		
	EP 705333	A1	19960410	EP 1994-917777	19940624
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08511688	T2	19961210	JP 1994-502622	19940624
	US 6025540	A	20000215	US 1995-556965	19951207
PRAI	DK 1993-753		19930624		
	WO 1994-IB181		19940624		

=> d au ti so ab 49-66 14

L4 ANSWER 49 OF 66 MEDLINE DUPLICATE 17

AU Kolb A F; Albang R; Brem G; Erfile V; Gunzburg W H; Salmons B

TI Characterization of a protein that binds a negative regulatory element in the mammary-specific **whey acidic protein promoter**.

SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1995 Dec 26) 217 (3) 1045-52.

Journal code: 0372516. ISSN: 0006-291X.

AB Whey Acidic Protein (WAP) gene expression is restricted to the pregnant and lactating mammary gland. We have recently defined a negative regulatory element (**NRE**) in the **WAP promoter** which interacts with a factor (NBF) present in all nonWAP expressing cells

(Kolb et al., 1994; J. Cell. Biochem. 56:245-261). Here we characterise this factor and show that although it is not related to a number of known transcription factors, including AP-1, NF-1 and SP-1, it may also be involved in controlling the expression from the mouse mammary tumour **virus** promoter. Three proteins that bind to the **WAP-NRE** have been identified, one of which is a 53kDa nuclear protein. This protein is present in nonWAP expressing cells, suggesting that it is responsible for limiting WAP expression to the pregnant and lactating mammary gland. This protein has been partially purified and its binding to the **WAP-NRE** is not appreciably affected by high salt concentrations.

- L4 ANSWER 50 OF 66 MEDLINE DUPLICATE 18  
 AU Petitclerc D; Attal J; Theron M C; Bearzotti M; Bolifraud P; Kann G; Stinnakre M G; Pointu H; Puissant C; Houdebine L M  
 TI The effect of various introns and transcription terminators on the efficiency of expression **vectors** in various cultured cell lines and in the mammary gland of transgenic mice.  
 SO JOURNAL OF BIOTECHNOLOGY, (1995 Jun 21) 40 (3) 169-78.  
 Journal code: 8411927. ISSN: 0168-1656.  
 AB Various combinations of promoters, introns and transcription terminators were used to drive the expression of bovine growth hormone (bGH) cDNA in different cell types. In constructs containing the human cytomegalovirus (hCMV) promoter and the SV40 late genes terminator, the intron from SV40 genes (VP1) was much more efficient, than the intron from the early genes (t). The synthetic intron SIS generated by the association of an adenovirus splice donor and an immunoglobulin G splice acceptor showed the highest activity. The respective potency of these introns was similar in several mammalian (CHO, HC11 and COS) and fish (TO2 and EPC) cells. The rabbit **whey acidic protein (WAP)** gene **promoter** was highly efficient to drive the expression of bGH gene in the HC11 mammary cell lines. In contrast, the bGH cDNA under the control of the same promoter was much less efficiently expressed when the SV40 VP1 intron and transcription terminator were used. The rabbit WAP gene and the human GH gene terminators did not or only moderately enhanced the expression of the construct WAP bGH cDNA. Introduction of a promoter sequence from the mouse mammary tumor **virus** (MMTV) LTR in the VP1 intron increased very significantly the expression of the WAP bGH cDNA. Although several of these **vectors** showed high potency when expressed stably in HC11 cells, all of them were only moderately efficient in transgenic mice. These data indicate that the VP1 and the SIS introns may be used to express foreign cDNAs with good efficiency in different cell types. The addition of an enhancer within an intron may still reinforce its efficiency. However, transfection experiments, even when stable expression is carried out, are poorly predictive of the potential efficiency of a **vector** in transgenic animals.
- L4 ANSWER 51 OF 66 MEDLINE DUPLICATE 19  
 AU Welte T; Garimorth K; Philipp S; Jennewein P; Huck C; Cato A C; Doppler W  
 TI Involvement of Ets-related proteins in hormone-independent mammary cell-specific gene expression.  
 SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1994 Aug 1) 223 (3) 997-1006.  
 Journal code: 0107600. ISSN: 0014-2956.  
 AB Regulatory regions have been located in the 5' flanking sequence of the mouse whey acidic protein gene which contribute to its tissue- and stage-specific expression in the mammary gland. They can be functionally separated into elements which mediate the action of lactogenic hormones prolactin and glucocorticoids and elements which control mammary cell-specific transcription in the absence of hormones. By mutational analysis, we have located a site in the **whey acidic protein promoter** between -120 and -100 which is important for hormone-independent promoter function. In stably transfected HC11 mammary epithelial cells, the hormone-independent activity of the mutated promoter was reduced 40-fold, whereas the capability to respond to

lactogenic hormones was retained. The site was specifically recognised by two nuclear factors contained in extracts of cultivated mammary epithelial cells or mammary glands. Electrophoretic mobility shift assay, DNase I footprinting and methylation interference experiments indicated a relation of both factors to the Ets family of DNA-binding proteins. One of these factors also recognised a functionally important site in the mammary cell-specific enhancer of the mouse mammary tumor **virus** long terminal repeat. The results suggest that factors related to the Ets family are important determinants in mammary cell-specific gene expression.

- L4 ANSWER 52 OF 66 MEDLINE DUPLICATE 20  
 AU Hennighausen L; McKnight R; Burdon T; Baik M; Wall R J; Smith G H  
 TI Whey acidic protein extrinsically expressed from the mouse mammary tumor **virus** long terminal repeat results in hyperplasia of the coagulation gland epithelium and impaired mammary development.  
 SO CELL GROWTH AND DIFFERENTIATION, (1994 Jun) 5 (6) 607-13.  
 Journal code: 9100024. ISSN: 1044-9523.  
 AB The whey acidic protein (WAP) is a milk protein that contains a cysteine-rich motif. This characteristic WAP signature has also been found in some protease inhibitors and certain proteins involved in tissue modeling. WAP is specifically synthesized in mammary tissue from late pregnant and lactating animals, and precocious synthesis results in impaired lobuloalveolar development of the gland in some transgenic lines. To determine whether growth modulatory effects of WAP are confined to mammary tissue, we expressed the WAP gene under the control of the mouse mammary tumor **virus** long terminal repeat in transgenic mice. The transgene was expressed at high levels in organs with exocrine function, such as mammary and salivary glands, prostate, seminal vesicle, and the coagulation gland. In addition to impaired mammary development, we observed hyperplasia and dysplasia of the coagulation gland epithelium. These findings suggest that WAP or a member of the WAP signature family can, in certain tissue contexts, function as an epithelial growth regulator. It appears from the present study that growth **regulatory** effects of **WAP** are restricted in the mouse to the mammary and coagulation gland epithelium.
- L4 ANSWER 53 OF 66 CAPLUS COPYRIGHT 2002 ACS  
 AU Kim, J. H.; Utsumi, K.; Iritani, A.; Lee, H. T.; Chung, K. S.  
 TI Characterization of morphological abnormalities in transgenic mice expressing the human erythropoietin gene  
 SO Molecules and Cells (1994), 4(4), 381-6  
 CODEN: MOCEEK; ISSN: 1016-8478  
 AB In previous studies, we found that overexpression of the human erythropoietin (hEPO) gene under the control of an exogenous promoter resulted in embryonic mortality on day 7 and day 17 of the gestation in transgenic mice. In this study, we have investigated the site of embryonic mortality caused by expression of the hEPO gene during development of the postimplantation stages in the transgenic embryos. Human EPO mRNA began to accumulate in amniotic sites on day 7 of gestation. Histol. anal. showed that amnion sites were degenerated in transgenic embryos exhibiting tissue-specific expression in the yolk sac. The highest embryonic death rate was found in gestation day 17. On embryonic day 17, embryos with the higher hEPO expression were more severely ruptured than those of the control or the low level of hEPO expression. According to the CAT assay, simian **virus** 40 and metallothionein promoters showed an 100-fold higher expression in preimplantation embryos than when acidic promoter did. These facts suggest that embryonic mortality in transgenic embryos is caused by overexpression of the human erythropoietin gene under the control of the exogenous promoter.
- L4 ANSWER 54 OF 66 SCISEARCH COPYRIGHT 2002 ISI (R)  
 AU KOLB A F; GUNZBURG W H; ALBANG R; BREM G; ERFLE V; SALMONS B (Reprint)

- TI **NEGATIVE REGULATORY ELEMENT IN THE MAMMARY SPECIFIC *WHEY***  
**ACIDIC PROTEIN PROMOTER**
- SO JOURNAL OF CELLULAR BIOCHEMISTRY, (OCT 1994) Vol. 56, No. 2, pp. 245-261.  
 ISSN: 0730-2312.
- AB Expression of the whey acidic protein (WAP) gene is tightly regulated in a tissue and developmental stage specific manner, in that the WAP gene is exclusively expressed in the mammary gland during pregnancy and lactation. Using both deletion and competition analyses, evidence is provided for the existence of a negative regulatory element (**NRE**) in the **WAP promoter** located between -413 and -93 with respect to the WAP transcriptional initiation site. This NRE dramatically decreases transcription from linked heterologous promoter-reporter gene constructs. The activity of **NRE** requires **WAP promoter** sequences that are 230 bp apart since subfragments of the NRE fail to inhibit transcription of adjoining reporter genes. Nuclear extracts from different cell types, in which the WAP gene is not active, contain a protein or complex that specifically interacts with the entire NRE but not with subfragments of it. The contact points between this protein (NRE binding factor [NBF]) and the NRE element have been partially determined. Mutation of the implicated nucleotides severely reduces the ability of NBF to bind, and such mutated promoter fragments fail to alleviate transcriptional repression in competition experiments. This suggests that NBF binding to the NRE is at least in part responsible for the negative regulation of the **WAP promoter**. Since NBF is not detectable in the lactating mammary gland, where the WAP gene is expressed, we speculate that it may be a determinant of the expression spectrum of the WAP gene. (C) 1994 Wiley-Liss, Inc.
- L4 ANSWER 55 OF 66 CAPLUS COPYRIGHT 2002 ACS
- IN Furth, Priscilla Anne; Hennighausen, Lothar
- TI Targeting gene expression to living tissue using jet injection
- SO PCT Int. Appl., 37 pp.  
 CODEN: PIXXD2
- AB A method for introduction of a DNA sequence encoding RNA and/or protein into the differentiated tissues of a living organism using a jet injector technique is presented. A flexible multi-nozzle injector device with a wide surface area to allow molding of the injector nozzle to the surface contours of the tissue is described. Addnl., an injection device having a long nozzle for injection of DNA deep into the host tissue is provided. Also, an injector device modified to be used with and/or inject through an endoscopic device is given. Three hybrid genes, i.e., the human cytomegalovirus immediate early gene 1 enhancer/promoter fused to the bacterial chloramphenicol acetyltransferase (CAT) or .beta.-galactosidase gene and the **whey acidic protein promoter** fused to the CAT gene, were injected into various mouse tissues by the jet injection technique. Minimal morbidity and pain was assocd. with the injection. CAT or .beta.-galactosidase activity was obsd. in the injected tissue.
- L4 ANSWER 56 OF 66 CAPLUS COPYRIGHT 2002 ACS
- IN Hansson, Lennart; Stroemqvist, Mats; Bergstroem, Sven; Hernell, Olle; Toernell, Jan
- TI DNA encoding .kappa.-casein, manufacture of the protein with recombinant cells or transgenic mammals, and milk or infant formula containing the protein
- SO PCT Int. Appl., 124 pp.  
 CODEN: PIXXD2
- AB The human .kappa.-casein gene and cDNA are cloned and sequenced. .kappa.-Casein produced by expression of the cDNA or gene in recombinant cells or or transgenic mammals can be used to prep. infant formula (no data). E. coli transformed with expression **vector** pS425, contg. human .kappa.-casein cDNA fused to the heat-stable enterotoxin II signal sequence and the T7 promoter, produced .kappa.-casein. A bovine papilloma

virus I-derived vector was prepd. and used to prep.  
.kappa.-casein-producing CHO and C127 cells. Transgenic female mice which secreted .kappa.-casein into their milk were also produced.

- ✓ L4 ANSWER 57 OF 66 MEDLINE DUPLICATE 21  
AU Mehig C S; Elias V D; Mehig R J; Helferich W G; Tucker H A  
TI Development of a recombinant bovine leukemia **virus**  
**vector** for delivery of a synthetic bovine growth hormone-releasing  
factor gene into bovine cells.  
SO JOURNAL OF ANIMAL SCIENCE, (1993 Mar) 71 (3) 687-93.  
Journal code: 8003002. ISSN: 0021-8812.  
AB Continuous intravenous infusion of bovine growth hormone-releasing factor  
(bGRF) increases milk synthesis in dairy cattle by as much as 46%. We have  
begun to develop a system for delivery and expression of a synthetic bGRF  
gene in cultured bovine cells using the provirus of the bovine leukemia  
**virus** (BLV). The gene encoding synthetic bGRF, constructed from  
eight overlapping oligonucleotides, was fused to the **whey**  
**acidic protein promoter** (WAP) or the  
mouse mammary tumor **virus** promoter (MMTV). These plasmids,  
termed pWAP.GRF and pMMTV.GRF, were able to induce transcription of bGRF  
upon transfection into Madin-Darby bovine kidney (MDBK) cells and  
induction with a lactogenic hormonal milieu (prolactin, hydrocortisone,  
triiodothyronine, insulin) or dexamethasone. When these constructs were  
cloned into a BLV **vector** in place of its oncogenic region, and  
transfected into MDBK cells, bGRF was expressed. **Virus**  
**particles** were prepared from these cultures and used to deliver  
the bGRF gene by viral infection into fresh MDBK cells. Northern blot  
analysis of MDBK total RNA revealed a fivefold higher level of expression  
of bGRF mRNA in transfected cultures than in virally infected cells, and  
no expression was detected in control cultures. The bGRF peptide was  
detected in both cell extracts and media samples from transfected cultures  
but was not detected in cell extracts or media samples from virally  
infected cells. This provirus construct may prove useful as a delivery  
system for peptides into cattle.
- L4 ANSWER 58 OF 66 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
AU Cardiff, Robert D. (1); Muller, William J.  
TI Transgenic mouse models of mammary tumorigenesis.  
SO Lemoine, N. R. [Editor]; Wright, N. A. [Editor]. Cancer Surveys, (1993)  
Vol. 16, pp. 97-113. Cancer Surveys; The molecular pathology of cancer.  
Publisher: Cold Spring Harbor Laboratory Press 10 Skyline Drive,  
Plainview, New York 11803, USA.  
ISSN: 0261-2429. ISBN: 0-87969-389-4.
- L4 ANSWER 59 OF 66 SCISEARCH COPYRIGHT 2002 ISI (R)  
AU WELTE T; PHILIPP S; CAIRNS C; GUSTAFSSON J A; DOPPLER W (Reprint)  
TI GLUCOCORTICOID RECEPTOR-BINDING SITES IN THE PROMOTER REGION OF MILK  
PROTEIN GENES  
SO JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, (DEC 1993) Vol. 47,  
No. 1-6, pp. 75-81.  
ISSN: 0960-0760.  
AB The action of glucocorticoids on the induction of the two milk protein  
genes beta-casein and whey acidic protein (WAP) is delayed and appears to  
be indirect. The response requires a co-stimulation of cells with  
prolactin, is restricted to mammary epithelial cells and is dependent on  
cis-acting sequences localized in the promoter region of the two genes. We  
have searched for glucocorticoid receptor (GR) binding sites in these  
hormone response regions. In vitro DNaseI footprinting experiments were  
performed with a purified preparation of the GR from rat liver. The  
sequences between -231 and -7 and between -250 and -79 of mouse WAP and  
rat beta-casein gene promoter, respectively, were found to contain  
multiple sites which were protected from the attack of DNaseI by the GR  
preparation. The sites comprise sequence motifs related to the delayed  
secondary glucocorticoid response elements described (Chan et al., J.

Biol. Chem. 266, 22,634-22,644, 1991), which represent half sites of classical GR binding sites. In the **WAP** gene promoter, the motifs are arranged head to tail with irregular spacing. The GR binding sites are in close proximity or even overlap with the binding sites for candidate factors involved in mammary cell specific gene expression. The results suggest a direct co-operation between GR and mammary cell specific transcription factors in mediating the expression of milk protein genes.

- L4 ANSWER 60 OF 66 CAPLUS COPYRIGHT 2002 ACS  
AU Dale, Trevor C.; Krnacik, Michael J.; Schmidhauser, Christian; Yang, Claudia L. Q.; Bissell, Mina J.; Rosen, Jeffrey M.  
TI High-level expression of the rat whey acidic protein gene is mediated by elements in the promoter and 3' untranslated region  
SO Molecular and Cellular Biology (1992), 12(3), 905-14  
CODEN: MCEBD4; ISSN: 0270-7306  
AB The high-level expression of the rat whey acidic protein (WAP) gene in transgenic mice depends on the interaction of 5'-flanking promoter sequences and intragenic sequences. Constructs contg. 949 bp of promoter sequences and only 70 bp of 3'-flanking DNA were expressed at uniformly high levels, comparable to or higher than that of the endogenous gene. Although this WAP transgene was developmentally regulated, it was expressed earlier during pregnancy than was the endogenous WAP gene. Replacement of 3' sequences, including the WAP poly(A) addn. site, with simian virus 40 late poly(A) sequences resulted in an .apprx.20-fold redn. in the expression of WAP mRNA in the mammary gland during lactation. Nevertheless, position-independent expression of the transgene was still obsd. Further deletion of 91 bp of conserved WAP 3' untranslated region (UTR) led to integration site-dependent expression. Position independence was restored following reinsertion of the WAP 3' UTR into the deleted construct at the same location, but only when the insertion was in the sense orientation. The marked differences obsd. between the expression levels of the 3'-end deletion constructs in transgenic mice were not seen in transfected CID 9 mammary epithelial cells. In these cells, expression of the endogenous WAP gene was dependent on the interaction of these cells with a complex extracellular matrix. In contrast, the transfected WAP constructs were not dependent on extracellular matrix for expression. Thus, both the abnormal expression of WAP in cells cultured on plastic and the precocious developmental expression of WAP in transgenic mice may reflect the absence of a neg. control element(s) within these recombinant constructs.
- L4 ANSWER 61 OF 66 MEDLINE DUPLICATE 22  
AU Ebert K M; Selgrath J P; DiTullio P; Denman J; Smith T E; Memon M A; Schindler J E; Monastersky G M; Vitale J A; Gordon K  
TI Transgenic production of a variant of human tissue-type plasminogen activator in goat milk: generation of transgenic goats and analysis of expression.  
SO BIO/TECHNOLOGY, (1991 Sep) 9 (9) 835-8.  
Journal code: 8309273. ISSN: 0733-222X.  
AB We report the first successful production of transgenic goats that express a heterologous protein in their milk. The production of a glycosylation variant of human tPA (LATPA--longer acting tissue plasminogen activator) from an expression vector containing the murine whey acid promoter (WAP) operatively linked to the cDNA of a modified version of human tPA was examined in transgenic dairy goats. Two transgenic goats were identified from 29 animals born. The first animal, a female, was mated and allowed to carry the pregnancy to term. Milk was obtained upon parturition and was shown to contain enzymatically active LATPA at a concentration of 3 micrograms/ml.
- L4 ANSWER 62 OF 66 SCISEARCH COPYRIGHT 2002 ISI (R)  
AU GUNZBURG W H; SALMONS B (Reprint); ZIMMERMANN B; MULLER M; ERFLE V; BREM G  
TI A MAMMARY-SPECIFIC PROMOTER DIRECTS EXPRESSION OF GROWTH-HORMONE NOT ONLY

SO TO THE MAMMARY-GLAND, BUT ALSO TO BERGMAN GLIA CELLS IN TRANSGENIC MICE  
MOLECULAR ENDOCRINOLOGY, (1991) Vol. 5, No. 1, pp. 123-133.

AB The **whey acidic protein (WAP)**

**promoter** has been previously used to target the expression of heterologous genes to the mammary glands of transgenic mice. To direct the expression of human GH (hGH) to mouse mammary glands, hGH-coding sequences have been coupled to **WAP promoter** sequences (**WAP-hGH**). Female transgenic mice carrying the WAP-hGH constructs show expression of hGH in the mammary gland, demonstrating the functionality of the transgenes. However, when other organs from these transgenic mice were examined, high level expression of hGH was unexpectedly observed in the brains of all male and female mice. Using in situ hybridization or immunohistochemistry, hGH expression from the transgene was seen to occur specifically in Bergman glia cells. In contrast, mice carrying hGH-coding sequences linked to the metallothionein promoter do not express hGH in these cells. Neither the endogenous WAP gene nor at least three other transgenes in which heterologous genes have been placed under the transcriptional control of the **WAP promoter** are expressed in the brain. Thus, we propose that the combination of the **WAP promoter** and the hGH structural gene results in a novel tissue specificity in the Bergman glia.

L4 ANSWER 63 OF 66 CAPLUS COPYRIGHT 2002 ACS

AU Henninghausen, Lothar; Furth, Priscilla A.; Pittius, Christoph W.

TI .kappa.B elements strongly activate gene expression in non-lymphoid cells and function synergistically with NF1 elements

SO Nucleic Acids Research (1989), 17(20), 8197-206

CODEN: NARHAD; ISSN: 0305-1048

AB .kappa.B elements have been described as lymphoid-specific transcriptional activators. .kappa.B elements are able to stimulate expression from test promoters more than 100-fold in T47D and 3T3 non-lymphoid cells. Nuclear proteins from T47D cells form two prominent complexes with HIV .kappa.B sites. Since the complexes formed in nuclear exts. from T47D and PHA/PMA stimulated Jurkat cells comigrate in polyacrylamide gels, it is suggested that the resp. binding protein in T47D cells is either NF-.kappa.B or a closely related family member. NF1 and .kappa.B elements can act synergistically to further increase transcriptional activity.

L4 ANSWER 64 OF 66 CAPLUS COPYRIGHT 2002 ACS

AU Gordon, Katherine; Vitale, James; Lee, Eric; Westphal, Heiner; Hennighausen, Lothar

TI Expression of human TPA in the milk of transgenic animals

SO UCLA Symposia on Molecular and Cellular Biology, New Series (1989), 87(Gene Transfer Gene Ther.), 57-66

CODEN: USMBD6; ISSN: 0735-9543

AB A series of transgenic mice which contain a mammary-specific expression cassette were produced in order to target prodn. of tissue plasminogen activator (TPA) to the lactating mammary gland. The fusion construct contained the promoter from the murine whey acid protein (WAP) gene and the secretion signal and coding segment of the TPA gene. Biol. active human TPA was secreted into milk in all transgenic lineages which expressed product, though there was much variability in expression levels among the different lineages. The WAP-TPA expression **vector** appears to be expressed and regulated properly, providing a model system for the prodn. of active proteins in the mammary gland.

L4 ANSWER 65 OF 66 MEDLINE

AU Pittius C W; Hennighausen L; Lee E; Westphal H; Nicols E; Vitale J; Gordon K

TI A milk protein gene promoter directs the expression of human tissue plasminogen activator cDNA to the mammary gland in transgenic mice.

SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1988 Aug) 85 (16) 5874-8.

Journal code: 7505876. ISSN: 0027-8424.

AB Whey acidic protein (WAP) is a major whey protein in mouse milk. Its gene is expressed in the lactating mammary gland and is inducible by steroid and peptide hormones. A series of transgenic mice containing a hybrid gene in which human tissue plasminogen activator (tPA) cDNA is under the control of the murine **WAP gene promoter** had previously been generated. In this study, 21 tissues from lactating and virgin transgenic female mice containing the WAP-tPA hybrid gene were screened for the distribution of murine WAP and human tPA transcripts. Like the endogenous WAP RNA, WAP-tPA RNA was expressed predominantly in mammary gland tissue and appeared to be inducible by lactation. Whereas WAP transcripts were not detected in 22 tissues of virgin mice, low levels of WAP-tPA RNA, which were not modulated during lactation, were found in tongue, kidney, and sublingual gland. These studies demonstrate that the **WAP gene promoter** can target the expression of a transgene to the mammary gland and that this expression is inducible during lactation.

L4 ANSWER 66 OF 66 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AU Attal, Joe; Cajero-Juarez, Marco; Petitclerc, Denis; Theron, Marie-Claire; Stinnakre, Marie-Georges; Bearzotti, Monique; Kann, Guy; Houdebine, Louis-Marie (1)

TI The effect of matrix attached regions (MAR) and specialized chromatin structure (SCS) on the expression of gene constructs in cultured cells and in transgenic mice.

SO Molecular Biology Reports, Vol. 22, No. 1, pp. 37-46.  
ISSN: 0301-4851.

AB The flanking sequences of several genes have been shown to direct a position independent expression of transgenes. Attempts to completely identify the insulating sequences have failed so far. Some of these sequences contain a matrix attached region (MAR) located in the flanking part of the genes. This article will show that the MARs in cultured cells located in the 3' OH region of the human apolipoprotein B100 (Apo B100) and within the SV40 genome were unable to stimulate and insulate transgene expression directed by the **promoters** from a rabbit **whey acidic protein (WAP) gene** or from human cytomegalovirus (hCMV) early genes. In transgenic mice, the MAR from the Apo B100 and SV40 genes did not enhance the expression of a transgene containing the rabbit whey acid protein (**WAP promoter**), the late gene SV40 intron (VP1 intron), the bovine growth hormone (bGH) cDNA and the SV40 late gene terminator. This construct was even toxic for embryos. Similarly, the specialized chromatin structure (SCS) from the Drosophila 87A7 HSP70 gene reduced chloramphenicol acetyl transferase (CAT) activity when added between a cytomegalovirus (CMV) enhancer and a Herpes simplex thymidine kinase (TK) gene promoter. This inhibitory action was almost complete when a second SCS sequence was added before the CMV enhancer. Sequences from the firefly luciferase and from the human gene cathepsin D cDNA used as control unexpectedly showed a similar inhibitory effect when added to the CMVTKCAT construct instead of SCS. When added before the CMV enhancer and after the transcription terminator in the CMVTKCAT construct, the SCS sequence was unable to insulate the integrated gene as seen by the fact that the level of CAT in cell extracts were by no means correlated with the number of copies in individual clones. From these data, it is concluded that i) a MAR containing the canonical AT rich sequences does not amplify the expression of all gene constructs ii) AT rich MAR sequences do not have per se an insulating effect iii) Drosophila SCS from the 87A7 HSP70 gene has no insulating effect in all gene constructs (at least in mammalian cells) iv) and the addition of a DNA fragment between an enhancer and a promoter in a gene construct cannot be used as a reliable test to evaluate its insulating property.

=> s (retrovirus or retroviral) and l4

L5 9 (RETROVIRUS OR RETROVIRAL) AND L4



=> d au ti so 1-9 15

- L5 ANSWER 1 OF 9 MEDLINE  
AU Ozturk-Winder Feride; Renner Matthias; Klein Dieter; Muller Mathias;  
Salmons Brian; Gunzburg Walter H  
TI The murine **whey acidic protein promoter** directs expression to human mammary tumors after **retroviral** transduction.  
SO CANCER GENE THERAPY, (2002 May) 9 (5) 421-31.  
Journal code: 9432230. ISSN: 0929-1903.
- L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2002 ACS  
IN Hodgson, Clague P.  
TI Retrotransposon **vectors** for gene transfer  
SO U.S., 49 pp., Cont.-in-part of U.S. Ser. No. 194,208, abandoned.  
CODEN: USXXAM
- L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2002 ACS  
IN Black, Margaret E.  
TI Thymidine kinase mutants and fusion proteins having thymidine kinase and guanylate kinase activities  
SO PCT Int. Appl., 126 pp.  
CODEN: PIXXD2
- L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS  
IN Loeb, Lawrence A.; Black, Margaret E.  
TI Thymidine kinase mutants with increased activity, **vectors** expressing mutants, and pharmacological uses  
SO U.S., 72 pp., Cont.-in-part of U.S. Ser. No. 237,592, abandoned.  
CODEN: USXXAM
- L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2002 ACS  
IN Gunzburg, Walter H.; Karle, Peter; Saller, Robert Michael  
TI Cytochrome P450 encoding **retroviral vectors** and their use as antitumor agents  
SO PCT Int. Appl., 25 pp.  
CODEN: PIXXD2
- L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2002 ACS  
IN Guenzburg, Walter H.; Saller, Robert Michael; Salmons, Brian  
TI Rodent whey acid protein (WAP) or mouse mammary tumor **virus** (MMTV) regulatory sequences for targeted expression of heterologous genes in human mammary cells and applications in carcinoma gene therapy  
SO PCT Int. Appl., 46 pp.  
CODEN: PIXXD2
- L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS  
IN Guenzburg, Walter H.; Winder, David; Saller, Robert Michael  
TI **Vectors** carrying therapeutic genes encoding antimicrobial peptides for gene therapy  
SO PCT Int. Appl., 54 pp.  
CODEN: PIXXD2
- L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2002 ACS  
IN Guenzburg, Walter H.; Salmons, Brian  
TI Viral and plasmid **vectors** encoding mouse mammary tumor **virus** Naf repressor or Sag antigen for control of viral infections or lymphocyte gene therapy  
SO PCT Int. Appl., 44 pp.  
CODEN: PIXXD2
- L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2002 ACS  
IN Guenzburg, Walter Henry; Saller, Robert Michael  
TI Safe, non-self-inactivating **retroviral** expression

**vectors** using non-LTR promoters for gene therapy  
SO PCT Int. Appl., 40 pp.  
CODEN: PIXXD2

=> d bib 7-9 15

L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS  
AN 1996:661120 CAPLUS  
DN 125:294754  
TI **Vectors** carrying therapeutic genes encoding antimicrobial  
peptides for gene therapy  
IN Guenzburg, Walter H.; Winder, David; Saller, Robert Michael  
PA Bavarian Nordic, Den.; GSF-Forschungszentrum fuer Umwelt und Gesundheit  
GmbH  
SO PCT Int. Appl., 54 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9628563	A1	19960919	WO 1996-EP1001	19960308
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9651039	A1	19961002	AU 1996-51039	19960308
	EP 817858	A1	19980114	EP 1996-907398	19960308
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
	JP 11503305	T2	19990326	JP 1996-527259	19960308
PRAI	DK 1995-243		19950309		
	WO 1996-EP1001		19960308		

L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2002 ACS  
AN 1996:661119 CAPLUS  
DN 125:294771  
TI Viral and plasmid **vectors** encoding mouse mammary tumor  
**virus** Naf repressor or Sag antigen for control of viral infections  
or lymphocyte gene therapy  
IN Guenzburg, Walter H.; Salmons, Brian  
PA Bavarian Nordic Research Institute A/s, Den.; GSF-Forschungszentrum fuer  
Umwelt und Gesundheit GmbH  
SO PCT Int. Appl., 44 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9628564	A1	19960919	WO 1996-EP1002	19960308
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9651040	A1	19961002	AU 1996-51040	19960308
	EP 817859	A1	19980114	EP 1996-907399	19960308

EP 817859 B1 20020116  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI  
 JP 11508441 T2 19990727 JP 1996-527260 19960308  
 EP 1162273 A1 20011212 EP 2001-118945 19960308  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI  
 AT 212061 E 20020215 AT 1996-907399 19960308  
 US 2002061297 A1 20020523 US 2001-965135 20010927  
 PRAI DK 1995-244 A 19950309  
 DK 1995-DK244 A 19950309  
 EP 1996-907399 A3 19960308  
 WO 1996-EP1002 W 19960308  
 US 1997-925214 A2 19970908

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2002 ACS  
 AN 1996:346074 CAPLUS  
 DN 125:2982  
 TI Safe, non-self-inactivating **retroviral** expression  
**vectors** using non-LTR promoters for gene therapy  
 IN Guenzburg, Walter Henry; Saller, Robert Michael  
 PA GSF-Forschungszentrum fuer Umwelt und Gesundheit GmbH, Germany  
 SO PCT Int. Appl., 40 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9607748	A1	19960314	WO 1995-EP3445	19950901
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE,				
	KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL,				
	RO, RU, SD, SG, SI, SK, TJ, TT, UA, UG, US, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,				
	LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,				
	SN, TD, TG				
	CA 2198210	AA	19960314	CA 1995-2198210	19950901
	AU 9535201	A1	19960327	AU 1995-35201	19950901
	AU 688590	B2	19980312		
	EP 779929	A1	19970625	EP 1995-931969	19950901
	EP 779929	B1	20010411		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1159210	A	19970910	CN 1995-194903	19950901
	BR 9508664	A	19980106	BR 1995-8664	19950901
	HU 76974	A2	19980128	HU 1997-1764	19950901
	JP 10507628	T2	19980728	JP 1995-509186	19950901
	AT 200517	E	20010415	AT 1995-931969	19950901
	ES 2156945	T3	20010801	ES 1995-931969	19950901
	NO 9700902	A	19970424	NO 1997-902	19970227
	FI 9700892	A	19970228	FI 1997-892	19970228
PRAI	DK 1994-1017	A	19940902		
	WO 1995-EP3445	W	19950901		

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